

WHAT IS CLAIMED IS:

1 A pharmaceutical composition in dosage unit form adapted for modulation of excitable tissue, enhancement of cognitive function or delivery of compounds across

5 endothelial tight junctions which comprises, per dosage unit, an effective non-toxic amount within the range from about 50,000 to 500,000 Units of EPO, an EPO receptor activity modulator, an EPO-activated receptor modulator, or a combination thereof, and a pharmaceutically acceptable carrier.

10 2. The pharmaceutical composition of Claim 1, wherein the effective non-toxic amount of EPO comprises 50,000 to 500,000 Units of EPO.

15 3. The pharmaceutical composition of Claim 1, wherein the effective non-toxic amount of EPO is a dose effective to achieve a circulating level of EPO of greater than 10,000 mU/ml of serum.

20 4. The pharmaceutical composition of Claim 3, wherein the circulating level of EPO is measured at about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 hours after the administration of EPO.

5. A pharmaceutical kit with one or more containers comprising the pharmaceutical composition of Claim 2.

25 6. A method for the protection of a mammal from pathology resulting from injury to excitable tissue comprising administering peripherally to said mammal an effective amount of EPO, an EPO receptor activity modulator, or an EPO-activated receptor modulator, for the protection of an excitable tissue.

30 7. The method of Claim 6 wherein said injury is the result of a seizure disorder, multiple sclerosis, stroke, hypotension, cardiac arrest, ischemia, myocardial infarction, inflammation, age-related loss of cognitive function, radiation damage, cerebral palsy, neurodegenerative disease, Alzheimer's disease, Parkinson's disease, Leigh disease, AIDS dementia, memory loss, amyotrophic lateral sclerosis, alcoholism, mood disorder, anxiety disorder, attention deficit disorder, autism, Creutzfeld-Jakob disease, brain or spinal cord

35 trauma, heart-lung bypass, glaucoma, retinal ischemia, or retinal trauma.

8. The method of Claim 6 wherein said injury is a result of hypoxia.

9. The method of Claim 8 wherein said hypoxia is prenatal or postnatal oxygen deprivation, suffocation, choking, near drowning, post-surgical cognitive dysfunction, 5 carbon monoxide poisoning, smoke inhalation, chronic obstructive pulmonary disease, emphysema, adult respiratory distress syndrome, hypotensive shock, septic shock, anaphylactic shock, insulin shock, sickle cell crisis, cardiac arrest, dysrhythmia, nitrogen narcosis, or localized tissue hypoxia.

10 10. A method for enhancing the function of normal or abnormal excitable tissue in a mammal comprising administering peripherally to said mammal a peripherally effective excitable tissue enhancing amount of an EPO, an EPO receptor activity modulator, an EPO-activated receptor modulator, or combination thereof.

15 11. The method of Claim 10 wherein said enhancing the function of excitable tissue results in the enhancement of associative learning or memory.

12. The method of Claim 10 wherein said enhancing the function of excitable tissue is used in the treatment of mood disorders, anxiety disorders, depression, autism, 20 attention deficit hyperactivity disorder, Alzheimer's disease, aging or cognitive dysfunction.

13. The method of Claim 6 or 10 wherein said excitable tissue is central nervous system tissue, peripheral nervous system tissue or heart tissue.

25 14. The method of Claim 6 or 10 wherein said administration comprises oral, topical, intraluminal or by inhalation or parenteral administration.

15. The method of Claim 14 wherein said parenteral administration is intravenous, intraarterial, subcutaneous, intramuscular, intraperitoneal, submucosal or 30 intradermal.

16. The method of Claim 6 or 10 wherein said administration is acute or chronic.

17. The method of Claim 6 or 10 wherein said EPO is nonerythropoietic.

18. The method of Claim 6 or 10 wherein said EPO is administered at a dose greater than the dose necessary to maximally stimulate erythropoiesis.

19. A method for facilitating the transcytosis of a molecule across an endothelial cell barrier in a mammal comprising administration to said mammal a composition comprising said molecule in association with an EPO, an EPO receptor activity modulator, an EPO-activated receptor modulator, or combination thereof.

20. The method of Claim 19 wherein said association is a labile covalent bond, a stable covalent bond, or a noncovalent association with a binding site for said molecule.

21. The method of Claim 19 wherein said endothelial cell barrier is the blood-brain barrier, the blood-eye barrier, the blood-testes barrier, the blood-ovary barrier or the blood-placenta barrier.

22. The method of Claim 19 wherein said molecule is a receptor agonist or antagonist hormone, a neurotrophic factor, an antimicrobial agent, a radiopharmaceutical, an antisense compound, an antibody, an immunosuppressant, a toxin, or an anti-cancer agent.

23. The method of Claim 6, 10, or 19 wherein said EPO is erythropoietin, an erythropoietin analog, an erythropoietin mimetic, an erythropoietin fragment, a hybrid erythropoietin molecule, an erythropoietin receptor-binding molecule, an erythropoietin agonist, a renal erythropoietin, a brain erythropoietin, an oligomer thereof, a multimer thereof, a mutein thereof, a congener thereof, a naturally-occurring form thereof, a synthetic form thereof, a recombinant form thereof, or a combination thereof.

24. The method of Claim 23 wherein said EPO receptor-binding molecule is an antibody to the erythropoietin receptor.

25. A composition for transporting a molecule via transcytosis across an endothelial cell barrier comprising said molecule in association with an EPO, an EPO receptor activity modulator, or an EPO-activated receptor modulator.

26. The composition of Claim 25 wherein said EPO is erythropoietin, an erythropoietin analog, an erythropoietin mimetic, an erythropoietin fragment, a hybrid

erythropoietin molecule, an erythropoietin receptor-binding molecule, an erythropoietin agonist, a renal erythropoietin, a brain erythropoietin, an oligomer thereof, a multimer thereof, a mutein thereof, a congener thereof, a naturally-occurring form thereof, a synthetic form thereof, a recombinant form thereof, or a combination thereof.

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27. The composition of ~~Claim 25~~ wherein said molecule is a receptor agonist or antagonist hormone, a neurotrophic factor, an antimicrobial agent, a radiopharmaceutical, an antisense compound, an antibody, an immunosuppressant, a toxin, or an anti-cancer agent.

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add b6

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